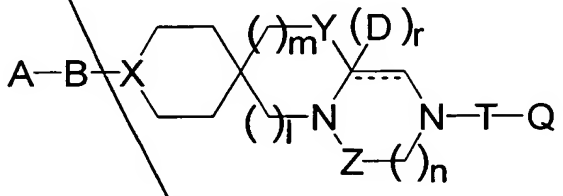
Claims:

1. A compound represented by formula (I) or its pharmaceutically acceptable salt



(I)

wherein A is a hydrogen atom, or

a group selected from (1) a saturated or unsaturated five- or six-membered cyclic hydrocarbon group, or a saturated or unsaturated five- or six-membered heterocyclic group, (2) an amino group, and (3) an imidoyl group (wherein the groups of (1) to (3) are optionally substituted);

B is a single bond, a carbonyl group, $-S(O)_x-$, or an optionally substituted C_{1-2} alkylene group;

D is a hydrogen atom, $-CO-R_5$ (wherein R_5 is a hydrogen atom or a substituent), or an optionally substituted C_{1-6} alkyl group;

X is a nitrogen atom or a methine group optionally substituted with a group A'-B'- (wherein A' represents a

group selected from those defined for A, and B' represents a group selected from those defined for B);

Y is an oxygen atom, $-S(O)_y-$, or an optionally substituted imino group (-NH-);

Z is a methylene group, a carbonyl group, or a thiocarbonyl group;

T is $-S(O)_z-$, a carbonyl group, or an optionally substituted C_{1-2} alkylene group;

Q is a hydrocarbon group or a heterocyclic group, which are optionally substituted;

l, m, n, x, y, and z are independently an integer selected from 0, 1 and 2 with the proviso that l and m are not simultaneously 0; and r is an integer of 0 or 1; and

the three rings (the ring containing X, the ring containing Y, and the ring containing Z) are independently optionally substituted; and the bond indicated by the broken line and the solid line in the ring containing Z is a single bond or a double bond (when r is 0).

2. At least one compound selected from the compounds as described below, or its (+) or (-) optical isomer, or its pharmaceutically acceptable salt:

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

(-)-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(hydroxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(ethoxycarbonylmethoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

6-(acetoxymethyl)-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-1'-(4-pyrimidinyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-((E)-4-chlorostyrylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(2-methoxyethoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(ethoxycarbonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one methanesulfone;

(-)-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(ethoxycarbonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

(-)-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(methoxycarbonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

(-)-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(isopropoxycarbonyl)-7-oxa-1'-(4-pyridyl) spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

(-)-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-6-(propoxycarbonyl)-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

(-)-6-(allyloxycarbonyl)-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

(-)-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(2-methoxyethoxycarbonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

(-)-1,4-diaza-6-(t-butoxycarbonyl)-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

ammonium 1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-2-oxo-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidine]-6-carboxylate;

(+)-ammonium 1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-2-oxo-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidine]-6-carboxylate;

(-)-ammonium 1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-2-oxo-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidine]-6-carboxylate;

4-[1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(methoxymethyl)-7-oxa-2-oxospiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-1'-yl]pyridine 1-oxide;

1'-acetimidoyl-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxaspiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

6-(aminomethyl)-1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(ethoxycarbonylaminomethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(morpholinomethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-methyl-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

ammonium 4-[1,4-diaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-oxa-2-oxo-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-6-yl]butylate;

1,4,7-triaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(methoxymethyl)-7-methyl-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(methoxymethyl)-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

(-)-1,4,7-triaza-4-(6-chloronaphthalen-2-ylsulfonyl)-6-(methoxymethyl)-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(7-chloro-2H-benzopyran-3-ylsulfonyl)-(6-methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(7-chloro-2H-benzopyran-3-ylmethyl)-(6-methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chlorobenzothiophen-2-ylsulfonyl)-(6-methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chlorobenzothiophen-2-ylmethyl)-(6-methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(5-chlorobenzofuran-2-ylsulfonyl)-(6-methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(5-chlorobenzofuran-2-ylmethyl)-(6-methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chlorobenzofuran-2-ylsulfonyl)-(6-methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(2H-benzopyran-3-sulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(7-chloro-2H-benzopyran-3-sulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(benzo[b]thiophen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(5-fluorobenzo[b]thiophen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(5-chlorobenzo[b]thiophen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chlorobenzo[b]thiophen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chloro-5-fluorobenzo[b]thiophen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(5-chloro-3-methylbenzo[b]thiophen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(5-chlorobenzo[b]furan-2-ylsulfonyl)-7-

oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(5-bromobenzo[b]furan-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(6-chlorobenzo[b]thiophen-2-ylsulfonyl)-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(5-chlorobenzo[b]furan-2-ylsulfonyl)-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(6-chlorobenzo[b]thiophen-2-ylsulfonyl)-7-methyl-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(5-chlorobenzo[b]furan-2-ylsulfonyl)-7-methyl-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(7-chloro-2H-benzopyran-3-sulfonyl)-6-(methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chlorobenzo[b]thiophen-2-ylsulfonyl)-6-(methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(5-chlorobenzo[b]furan-2-ylsulfonyl)-6-

(methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(6-chlorobenzo[b]thiophen-2-ylsulfonyl)-6-(methoxymethyl)-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(5-chlorobenzo[b]furan-2-ylsulfonyl)-6-(methoxymethyl)-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(6-chlorobenzo[b]thiophen-2-ylsulfonyl)-6-(methoxymethyl)-7-methyl-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(5-chlorobenzo[b]furan-2-ylsulfonyl)-6-(methoxymethyl)-7-methyl-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(6-chlorobenzo[b]furan-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(indol-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-[2-(5-chlorothiophen-2-yl)ethenesulfonyl]-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-[2-(5-chlorothiophen-2-yl)ethenesulfonyl]-1'-(4-

pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-[2-(5-chlorothiophen-2-yl)ethenesulfonyl]-7-methyl-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-[2-(5-chlorothiophen-2-yl)ethenesulfonyl]-6-(methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-[2-(5-chlorothiophen-2-yl)ethenesulfonyl]-6-(methoxymethyl)-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-[2-(5-chlorothiophen-2-yl)ethenesulfonyl]-6-(methoxymethyl)-7-methyl-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(naphthalen-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(2-chloroquinolin-6-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4-diaza-4-(5-ethynylbenzo[b]furan-2-ylsulfonyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(6-chloronaphthalen-2-ylsulfonyl)-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one;

1,4,7-triaza-4-(6-chloronaphthalen-2-ylsulfonyl)-7-methyl-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one, and

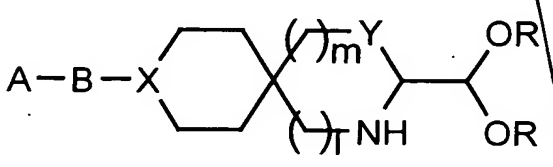
1,4-diaza-4-(2-chloroquinolin-6-ylsulfonyl)-6-(methoxymethyl)-7-oxa-1'-(4-pyridyl)spiro[bicyclo[4.3.0]nonane-8,4'-piperidin]-2-one.

3. A prodrug of the compound of claim 1 or 2 or its pharmaceutically acceptable salt.

4. A pharmaceutical composition characterized by that the composition contains a compound represented by formula (I) or its pharmaceutically acceptable salt as an effective component.

5. A FXa inhibitor characterized by that the inhibitor contains a compound represented by formula (I) or its pharmaceutically acceptable salt as an effective component.

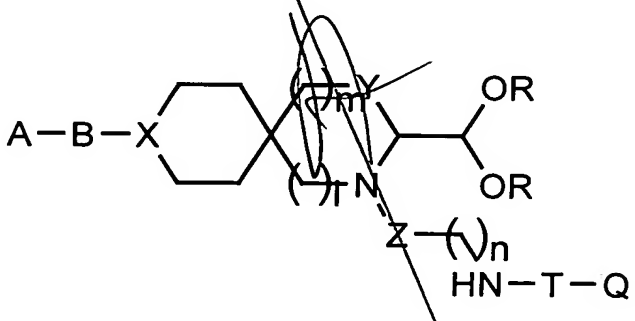
6. A compound represented by formula (V) or its salt



(V)

wherein A, B, X, Y, l, and m are as defined for the formula (I); the ring containing X and the ring containing Y are independently optionally substituted; and R is hydrogen atom, a C_{1-6} alkyl, a C_{1-6} alkoxy, or a C_{1-6} alkyl group optionally substituted with hydroxyl or a halogen atom, with the proviso that two R may together form a C_{1-6} alkyl, a C_{1-6} alkoxy, a C_{2-4} alkylene group optionally substituted with hydroxyl or a halogen atom.

7. A compound represented by formula (VI) or its salt

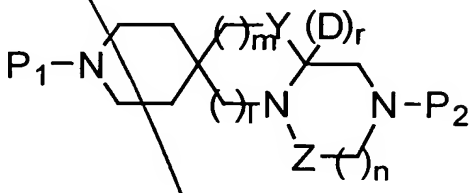


(VI)

wherein A, B, X, Y, Z, T, Q, l, m, and n are as defined for the formula (I); the ring containing X and the ring containing Y are independently optionally substituted; the alkylene chain which binds to Z when n is 1 or more is optionally substituted; and R is hydrogen atom, C_{1-6} alkyl, C_{1-6} alkoxy, a C1-6 alkyl group optionally substituted with hydroxyl or a halogen atom, with the proviso that two R may

together form a C_{1-6} alkyl, a C_{1-6} alkoxy, a C_{2-4} alkylene group optionally substituted with hydroxyl or a halogen atom.

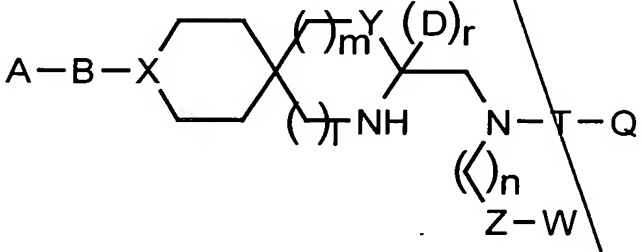
8. A compound represented by formula (Ik) or its salt



(I k)

wherein P_1 and P_2 independently represent hydrogen atom or a protective group for the imino group; Y, Z, D, l, m, n, and r are as defined for the formula (I); and the three rings are independently optionally substituted.

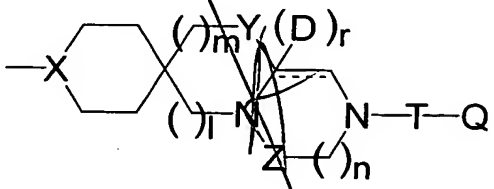
9. A compound represented by formula (I-a') or its salt



(I − a')

wherein A, B, D, X, Y, Z, Q, T, l, m, n, and r are as defined for the formula (I); W is a leaving group or a group convertible to a leaving group; the ring containing X and the ring containing Y are independently optionally substituted; and the alkylene which binds to Z when n is 1 or more is optionally substituted.

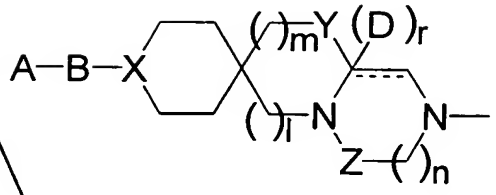
10. A compound exhibiting inhibitory activity for FXa which has a partial structure represented by formula (I'') in its molecule, or its pharmaceutically acceptable salt



(I'')

wherein -X= is -CH= or -N=; the three rings (the ring containing X, the ring containing Y, and the ring containing Z) are independently optionally substituted; Y, Z, D, T, Q, l, m, n, and r are as defined for the formula (I).

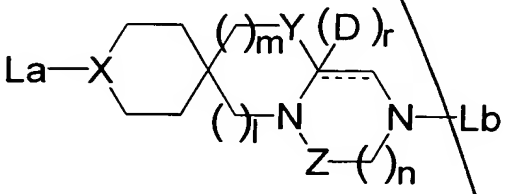
11. A compound exhibiting inhibitory activity for FXa which has a partial structure represented by formula (I''') in its molecule, or its pharmaceutically acceptable salt



(I''')

wherein X is a methine group or a nitrogen atom; the three rings (the ring containing X, the ring containing Y, and the ring containing Z) are independently optionally substituted; A, B, Y, Z, D, l, m, n, and r are as defined for formula (I).

12. A compound exhibiting inhibitory activity for FXa represented by the following formula (I'), or its pharmaceutically acceptable salt



(I')

wherein D is hydrogen atom, $-CO-R_5$ (wherein R_5 is hydrogen atom or a substituent), or an optionally substituted C_{1-6} alkyl group;

X is a methine group or a nitrogen atom;

Y is an oxygen atom, $-S(O)_y-$, or an optionally substituted imino group (-NH-);

the three rings (the ring containing X, the ring containing Y, and the ring containing Z) are independently optionally substituted;

Z is a methylene group, a carbonyl group, or a thiocarbonyl group;

l, m, n, and y are independently an integer selected from 0, 1 and 2 with the proviso that l and m are not simultaneously 0; and r is an integer of 0 or 1;

the bond indicated by the broken line and the solid line is a single bond or a double bond (when r is 0); and

La and Lb are groups involved in the binding of the compound of formula (I') with FXa, and

La represents a group which has a basic moiety which associates with S3 pocket of FXa [a space formed at least by amino acid residues Trp215, Phe174, Tyr99, Thr98, Glu97, and Lys96], and

Lb represents a group which has a hydrophobic moiety which binds to S1 pocket of FXa [a space formed at least by amino acid residues Val213, Ser214, Trp215, Gly216, Glu217, Gly218, Cys220, Asp189, Ala190, Cys191, Gln192, Gly193, Asp194, Ser195, Gly226, Ile227, and Tyr228], and which interacts with Tyr228 side chain in the S1 pocket but which

does not covalently bind to Ser195 in active center (wherein amino acid No. of the FXa is indicated by chymotrypsin No. used in Protein Data Bank (PDB), Registration ID: 1FAX (J. Biol. Chem. 1996 Nov. 22; 271(47): 29988-92)).

13. A compound which satisfies all of the conditions as descirbed below or its pharmaceutically acceptable salt

(1) the compound has a group including a basic moiety which associates with S3 pocket of FXa [a space formed at least by amino acid residues Trp215, Phe174, Tyr99, Thr98, Glu97, and Lys96] when the complex of the compound with FXa is in its crystalline state;

(2) the compound has a hydrophobic moiety which binds to S1 pocket of FXa [a space formed at least by amino acid residues Val213, Ser214, Trp215, Gly216, Glu217, Gly218, Cys220, Asp189, Ala190, Cys191, Gln192, Gly193, Asp194, Ser195, Gly226, Ile227, and Tyr228] when the complex is in its crystalline state;

(3) said hydrophobic moiety interacts with the Tyr228 side chain in the S1 pocket, while it does not covalently bind to the Ser195 in active center when the complex is in crystalline state; and

(4) the compound has inhibitory activity for FXa.

14. A pharmaceutical composition characterized by that the composition contains at least one compound or its pharmaceutically acceptable salt of claims 10 to 13 as an effective component.

15. A method for inhibiting FXa characterized by that the method comprises administration of the pharmaceutical composition of claim 14 to a mammal which requires inhibition of the FXa.

16. Crystal of a complex between FXa and at least one compound or its salt of claims 10 to 13.

17. A pharmacophore which is useful in identifying or designing an inhibitor which competitively binds to an active site of FXa or its fragment, and which satisfies all of (a) to (c):

(a) it is the three-dimensional structural parameter defining the binding mode when the inhibitor binds to S1 pocket of FXa by its hydrophobic moiety, and it induces interaction with Tyr228 side chain in S1 pocket;

(b) it is the three-dimensional structural parameter defining the binding mode when the inhibitor binds to S3 pocket of FXa by its basic moiety; and

(c) the inhibitor does not bind covalently to Ser195 in the active center.

18. A method for identifying or designing an inhibitor which competitively binds to an active site of FXa or its fragment, wherein the inhibitor is screened by providing three-dimensional structural information of the active site to a computer system; identifying a compound which is assumed to bind to the FXa in a manner satisfying all of the conditions that:

(a) the compound associates with S1 pocket by its hydrophobic moiety and the moiety interacts with Tyr228,

(b) the compound associates with the inside of S3 pocket of the active site by its basic moiety, and

(c) the compound does not bind covalently with Ser195; and

subjecting the compound to a biological assay which is capable of measuring FXa inhibitory activity to thereby determine whether the compound exhibits FXa inhibitory activity in the assay.

add A1